REMARKS

This amendment is submitted in an earnest effort to bring this application to issue without delay.

Applicants wish to reiterate their claim to the benefit of their Danish priority date of 25 November 2002 pursuant to the International Convention. A certified copy of Danish Patent Application PA 2002 01814 filed 25 November 2002 has already been made of record as part of Applicants' PCT/EP 2003/012610 filed 12 November 2003 of which th instant application is the US National Phase. Applicants respectfully request that the Examiner acknowledge Applicant's perfected right of priority.

Applicants have amended claim 23 to replace "the same" with "identical" so that the claim is no longer believed to be indefinite under 35 USC 112, second paragraph.

The Examiner has objected to claim 29 arguing that the Applicants' particular vaccinia virus Ankara vector, namely MVA-BN, is a trademarked composition, and as such the composition should be designated as a trademark. The Examiner has also asked that the Applicants' provide some information to indicate the common descriptive term for their MVA-BN since the composition of trademarked products can vary over time, where the same trademark is used to identify different products. Applicants, point out, however, that MVA-BN is the nomenclature used in biotechnology to describe this particular MVA strain and thus MVA-BN is the common descriptive term for this particular viral vector, and as such the

Examiner's fear that the name will be used in the future to identify products that are different from the present MVA-BN is unjustified.

The Examiner has also rejected claim 29 under 35 USC 112, first paragraph, on the grounds that the specification fails to comply with the written description and enablement clauses of this section of the statute. The Examiner is concerned that the Applicants' deposits of MVA-BN and MVA 575 have been made in accordance with the requirements of the Budapest Convention. Applicants enclose two Declarations of Deposit of Microorganism Under 37 CFR 1.808 identifying the Applicant to establish that a deposits of the microorganisms MVA-BN and MVA 575 have been made at a depository according to the requirements of the Budapest Convention, identifying the accession number, stating that all restrictions to the public for access to the deposit will be removed upon issuance of a patent, that access to the deposited material will be available to one determined by the Commissioner of Patents and Trademarks to have access to the material during the pendency of this application, that the depository will see to it that the deposit remains viable for at least five years since the last request for a sample, and for at least 30 years from the date of deposit, whichever is longer. Applicants also acknowledge the duty to replace the deposit should the depository be unable to furnish a sample. In view of the submission of this declaration, Applicants maintain that no rejection of claim 29 should be made under 35 USC 112, first paragraph, as based upon a specification

that fails to comply with either the written description clause or the enablement clause.

Applicants have canceled claim 33, without replacement, so the rejection of that claim under 35 USC 112, has become moot.

The Examiner has rejected claim 38 under 35 USC 101 as non-statutory and under 345 USC 112, second paragraph, as indefinite. Applicants believe that the Examiner meant to reject claim 35 on these grounds since claim 38 is a method of use claim that recites a positive method step. Rather claim 35 is directed to use of the new recombinant pox virus without including any positive steps. Applicants have canceled claim 35 so any such rejection has now become moot.

The Examiner has rejected claims 20 through 23, and 26 under 35 USC 112, first paragraph, as broader than the scope of the description of the invention provided by the specification. The Examiner has particularly pointed to several expressions in claim 20 including "derivative", "homology of at least 60%", "a sequence in which not more than 6 nucleotides are substituted, deleted, and/or inserted into SEQ ID No: 1", and "where a subsequence of the ATI promoter has a length of at least 10 nucleotides of the SEQ ID No: 1." Applicants believe that the Examiner should not maintain such a rejection against any claim now presented. In none of the claims now presented do Applicants define their ATI promoter either as a derivative of SEQ ID NO:1 nor as 60% homologous to SEQ ID No: 1. Nor do Applicants define the ATI promoter as a subsequence of the ATI promoter has a length of at least 10 nucleotides of the SEQ

ID No: 1. Applicants do provide as an alternative to SEQ ID No: 1, a polynucleotide having at least 10 nucleotides including nucleotides 22 through 29 of SEQ ID No: 1 and still active as an ATI promoter. Applicants also provide as an alternative to SEQ ID No:1, a polynucleotide sequence in which not more than 6 nucleotides are substituted, deleted, and/or inserted into SEQ ID No:1 and still active as an ATI promoter. These expressions and all other changes made to claims 20 through 23, 25 and 26 are fully supported by the specification on page 5, line 25 through page 8, line 29. All claims now presented are directed to a subgenus of ATI promoters in which Applicants are in possession, including SEQ ID NO:1 and a limited number of structurally similar promoters to SEQ ID No: 1 so as not to be beyond the description of invention provided by the specification.

Applicants emphasize that they have not invented the cowpox ATI promoter of SEQ ID NO:1 nor any of the fragments thereof nor structurally similar nucleotides having up to 6 different nucleotides substituted, deleted or inserted, nor any other novel polynucleotide. Applicants have not claimed any polynucleotide per se. The polynucleotide having SEQ ID NO:1 is in the prior art, and Applicants believe so are the structurally similar polynucleotides containing mutations. Applicants' invention is not the cowpox ATI promoter or similar polynucleotides, but rather is a recombinant poxvirus comprising in the viral genome at least two expression cassettes, each comprising a cowpox ATI promoter according to SEQ ID NO:1, a polynucleotide sequence in which not more than 6

nucleotides are deleted, substituted and/or inserted into SEQ ID NO:1, and still active as an ATI promoter, or a polynucleotide comprising a least 10 nucleotides including nucleotides 22 to 29 of SEQ ID NO:1, and still active as an ATI promoter. Since the cowpox ATI promoters are not the invention here, Applicants should not be held to the strict description requirement under 35 USC 112, first paragraph required for the disclosure of new compounds that are the subject of the invention. Accordingly the Vas-Cath decision cited by the Examiner on page 8 of the office action provides no legal basis for rejecting any claim now presented under 35 USC 112, first paragraph. Furthermore as explained hereinabove, Applicants have more sharply defined the cowpox ATI promoters in all claims now presented so as to be in full compliance with the description requirement of 35 USC 112, first paragraph.

On page 7 of the office action the Examiner indicates that to provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, method making the claimed product, or any combination thereof.

Applicants believe that the specification on page 5, line 25 through page 7, line 17 provides such an adequate written description of the genus of cowpox ATI promoters as now claimed. The structure of one species, that of SEQ ID NO:1, has been

completely identified. So has the partial structure of all species within the genus been identified, that is the structure is the same as that of SEQ ID NO:1 but may have up to 6 deletions, substitutions or additions. That disclosure certainly amounts to a disclosure of the partial structure of many of the species within the genus. In addition the species within the scope of the presently claimed genus may have at least 10 nucleotides in common with that of SEQ ID NO:1 and must include the nucleotides 22 to 29 of SEQ ID NO:1. Once again, here is more disclosure of partial structure of the remaining species within the genus as now claimed. Furthermore all claims now presented require that the species of cowpox ATI promoter within the genus all are active as ATI promoters.

The Examiner has cited Regents of the University of California V. Eli Lilly & Co., 43 USPQ 2d 1398 (CAFC 1997) for its holding that a description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of a genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. It is the latter provision of this holding that clearly applies to the present case and the present genus as defined in the claims now presented. Thus even though the polynucleotide that has SEQ ID NO:1 is the only species actually disclosed in the specification within the scope of the genus, the definition in the specification on pp 5 through 7 providing common structure and common function for all members of

the genus as now defined must be considered as well in determining whether the specification complies with the written description requirement under 35 USC 112, first paragraph, and whether the claims now presented are adequately supported by the specification.

On page 1406, right-hand column of the Regents of California decision the court referred to In re Grimme et al, 124 USPQ 499 (CCPA 1960). The Grimme et al decision essentially held that in considering the sufficiency of the disclosure of a specification to support a generic or subgeneric claim in the field of chemistry, the court has consistently held that the naming of one member of such a group is not, in itself, a proper basis for a claim to the entire group. However, it may not be necessary to enumerate a plurality of species if the genus is sufficiently identified in the application by other appropriate language. Applicants have already explained why in the present case, there is other appropriate language to identify the genus, the partial structure of SEQ ID NO: 1 that is common to all of the species within the genus as now defined and the common functionality of all of the species within the genus as now defined. Accordingly no rejection of any claim now presented should be maintained under 35 USC 112, first paragraph, as based upon a specification that fails to adequately describe the invention.

The Examiner has rejected claims 20 through 28, 31 through 35, and 41 under 35 USC 102 as anticipated by PICKUP et al (A). The Examiner argues that the reference discloses a recombinant poxvirus comprising at least two expression cassettes

including the ATI promoter and a coding sequence to be expressed. Furthermore the Examiner argues that the reference discloses that the same ATI promoter as Applicants' SEQ ID No: 1 may be included in the recombinant poxvirus and points to the polynucleotide in Figure 1 of the PICKUP reference that the Examiner contends is 100% homologous to Applicants' SEQ ID No: 1. The Examiner also points out that PICKUP discloses that the recombinant poxvirus may be used as a vector in the preparation of vaccines.

Applicants strongly disagree with the Examiner's view. PICKUP et al does not describe a recombinant poxvirus comprising in the viral genome at least two expression cassettes, each comprising the cowpox ATI promoter or structurally similar polynucleotides. PICKUP et al merely describes up-stream and downstream cis-acting elements of a poxvirus gene encoding the major protein component of the poxvirus A-type inclusion. A poxvirus comprising at least two expression cassettes each comprising the cowpox ATI promoter or structurally similar polynucleotide was NOT described.

The Examiner has pointed to Figure 1 of PICKUP et al which discloses the cis-acting element I (CAEI). The Examiner argues that this polynucleotide has the same structure as that of the ATI promoter of SEQ ID No: 1 according to the present invention. Applicants note that the stretch of polynucleotide in Fig. 1 between the two expressed portions of the polynucleotide does include the sequence GTTTTGAATAAAATTTTTTTATAATAAAT. However, that disclosure does not mean that the PICKUP reference either anticipates or renders the presently claimed invention.

Applicants' invention is not the discovery of the sequence of the polynucleotide that is the Cowpox ATI promoter. Applicants have discovered that at least two cassettes each containing the cowpox ATI promoter or a structurally similar polynucleotide as defined by the present claims, and followed by a coding polynucleotide, can efficiently and stably be expressed in a recombinant vaccinia virus vector according to the present invention, without the problem of instability caused by homologous recombination between the multiple ATI promoter regions. Nowhere in PICKUP is there disclosure of inserting into a poxviral vector at least two cassettes each containing the cowpox ATI promoter or a structurally similar polynucleotide as defined by the present claims, and followed by a coding polynucleotide. Nowhere in PICKUP is there any suggestion that such a viral vector would be stable without any risk of instability due to homologous recombination between the ATI promoters. Thus PICKUP per se provides no basis to reject any claim now presented as either anticipated under 35 USC 102 or as obvious under 35 USC 103.

PICKUP et al is irrelevant concerning the obviousness of the presently claimed invention since it merely describes the cis-acting elements (CAEI) of the poxvirus gene encoding the major protein component of the poxvirus A-type inclusion (ATI). A poxvirus comprising at least two CAEIs each controlling a coding sequence may not be found in the reference.

Nor does combining PICKUP with BLANCHARD et al provide any basis to reject any claim now presented as obvious under 35 USC

103. All that BLANCHARD et al discloses is that MVAs are highly useful forms of vaccinia virus for the preparation of human vaccines because the MVAs have a restricted host range, immunogenicity, and avirulence in animal test models, and an excellent safety record in smallpox vaccines. Applicants note that they have clearly described the novel and unobvious features of their invention hereinabove, and there is no suggestion of same to be found in PICKUP et al in combination with BLANCHARD et al. There is no suggestion in the combination of references to include multiple ATI promoters within a vaccinia followed by a coding sequence to enable stable expression of those coding sequences without instability of the virus due to homologous recombination of the multiple ATI promoter sites.

The closest prior art is HOWLEY et al Gene, [1996] 172, 233 through 237, cited on page 2 of the present application, which discloses recombinant Vaccinia viruses comprising one, two or three expression cassettes each comprising the p7.5 promoter. This reference was cited in the International Search Report (of record) prepared by the European Patent Office on 21 June 2004. Applicants now provide a copy in the event that the Examiner has not been able to obtain the International Search Report. HOWLEY et al. discloses that homologous recombination occurs in the recombinant viruses comprising two or three p7.5 promoters (see e.g. page 235, Fig. 2A, page 236, right column, lines 13 to 15, and page 237, conclusions (3)). Thus, the viruses as disclosed in HOWLEY et al. are genetically unstable.

The presently claimed invention relates to recombinant poxviruses comprising in the viral genome at least two expression cassettes, each comprising the cowpox ATI promoter having SEQ ID No: 1 or specifically defined polynucleotides of a similar structure either differing by up to 6 individual nucleotides, or including at least 10 nucleotides from SEQ ID No:1 and specifically nucleotides 22 through 29 of SEQ ID No: 1. All of the structurally closely related polynucleotides to the Cowpox ATI promoter of SEQ ID No: 1 have promoter activity. The comparative example on pages 16 through 22 of the present application shows that a recombinant poxvirus (mBN30) having two ATI promoter expression cassettes in the same insertion site in the MVA virus is stable showing good expression of the GUS gene under the control of the two ATI promoters, with no indication of homologous recombination and the resulting instability. See the table bridging pp 20 and 21 of the application. With a recombinant poxvirus (mBN31) having only one ATI promoter and one p7.5 promoter (the kind of promoter used in HOWLEY et al) the level of GUS gene expression was much lower indicating less stability.

Of course the HOWLEY et al reference discloses multiple insertions of p7.5 followed by coding sequences and the result is significant instability. Thus, the present invention differs from the disclosure of HOWLEY et al in that the recombinants comprising two ATI promoters are stable whereas the recombinants comprising two p7.5 promoters (HOWLEY et al) are unstable. There is no

disclosure or suggestion of such surprising stability to be found in any prior art reference.

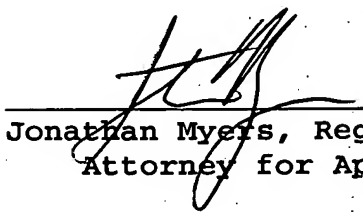
Consequently, the objective technical problem to be solved was the provision of stable recombinant poxviruses irrespective of the orientation comprising two or more expression cassettes the expression of which is controlled by the same or closely related promoter sequences.

Starting from HOWLEY et al the person skilled in the art would have believed that two identical sequences in the genome of a Vaccinia virus will always lead to instability of the virus. Indeed, there is no hint in HOWLEY et al or in any other document cited in the ISR that by replacing the p7.5 promoter with the ATI promoter stable recombinant viruses can be obtained that comprise at least two copies of the same promoter. Since it was unexpected that recombinant viruses comprising at least two ATI promoters are stable the subject matter of all claims now presented has to be regarded as both novel and inventive.

Applicants' undersigned representative would like to schedule a telephone interview with the Examiner some time after she has had a chance to consider this amendment.

Applicants believe that all claims now presented are in condition for allowance and a response to that effect is earnestly solicited.

Respectfully submitted,
The Firm of Karl F. Ross P.C.



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Enclosures: Abstract of the Disclosure
Declarations of Deposit of Microorganism
Howley reference